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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/785,793	02/16/2001	Bertrand Seraphin	70436	5538

22242 7590 11/03/2004

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EXAMINER	
HINES, JANA A	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 11/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/785,793	SERAPHIN ET AL.	
	Examiner	Art Unit	
	Ja-Na Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 July 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Amendment Entry

1. The amendment filed July 29, 2004 has been entered. Claims 1-5 have been amended. Claims 1-22 are pending in this office action.

Response to Arguments

2. Applicant's arguments filed July 29, 2004 have been fully considered but they are not persuasive.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. The scope of enablement rejection of claims 1-11 under 35 U.S.C. 112, first paragraph, is maintained for reasons already of record. The rejection was on the grounds that the specification is enabled for a method for detecting and/or purifying biomolecules and/or protein complexes from a yeast host, the method comprising: (a) providing a vector encoding a fusion of a yeast protein to the Calmodulin Binding Peptide-Tobacco Etch Virus protease NIA –Staphylococcus Protein A (CBP-TEV-Protein A) double tag wherein the fusion protein is one subunit of a protein complex of yeast containing 24 subunits and the plasmid is transformed in to the yeast cell; (b)

maintaining the expression environment under conditions that facilitate expression of the proteins in a native form which retains their biological activity as fusion proteins with affinity tags, and under conditions that allow the formation of a complex between the subunits; (c) purifying the one or more subunits by a combinations of at least two different affinity purification steps each comprising binding the one or more subunits via one affinity tag to a support material capable of selectively binding one of the affinity tags and separating the one or more subunits from the support material after substances not bound to the support material have been removed wherein the first affinity step allows purification by binding to IgG linked beads, eluting the TEV protease cleavage binding of the eluted material on calmodulin containing beads and the second affinity step comprises calmodulin affinity elution; (d) concentrating the eluted proteins using precipitation techniques; and (e) detecting the concentrated proteins by polyacrylamide gel electrophoreses.

The claims are not enabled for a method for detecting and/or purifying biomolecules and/or protein complexes, the method comprising: (a) providing an expression environment containing one or more heterologous nucleic acids encoding one or more subunits of a biomolecule complex; (b) maintaining the expression environment under conditions that facilitate expression of the one or more subunits in a native form as fusion proteins with subunits being fused to at least two different affinity tags, wherein one of the affinity tags consists of one or more IgG binding domains of Staphylococcus protein A; (c) purifying the one or more subunits by a combinations of at least two different affinity purification steps each comprising binding the one or more

subunits via one affinity tag to a support material capable of selectively binding one of the affinity tags and separating the one or more subunits from the support material after substances not bound to the support material have been removed to provide a purified biomolecule and/or protein complex; and (d) detecting the purified biomolecule and/or protein complex.

Applicants' merely assert that undue experimentation is not required based on factors like the quantity of experimentation, guidance presented, and working examples. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with these claims, contrary to applicants' arguments. The instant examples recite that a method comprises providing a vector encoding a fusion of a yeast protein to the Calmodulin Binding Peptide-Tobacco Etch Virus protease NIA –Staphylococcus Protein A (CBP-TEV-Protein A) double tag wherein the fusion protein is one subunit of a protein complex of yeast containing 24 subunits and the plasmid is transformed in to the yeast cell. There are no examples commensurate in scope to the broad claims. The claims are only enabled for complexes from a yeast host. The claims are only enabled for encoding a fusion of a yeast protein to the Calmodulin Binding Peptide-Tobacco Etch Virus protease NIA –Staphylococcus Protein A (CBP-TEV-Protein A) double tag wherein the fusion protein is one subunit of a protein complex of yeast containing 24 subunits and the plasmid is transformed in to the yeast cell. The claims are not enabled for providing a generic expression environment containing any type of heterologous nucleic acids encoding one or more subunits of a biomolecule complex, since this

includes unidentified heterologous nucleic acids. Also, the claims are only enabled when the method also comprises concentrating the eluted proteins using precipitation techniques; and detecting the concentrated proteins by polyacrylamide gel electrophoreses.

The teaching within the specification is limited to the specific steps and reagents recited in the instant specification. The specification fails to teach examples of detection and purify biomoleucles and protein complexes, such that without the exact and precise method steps and specific reagents the claimed detection and purification methods could not be achieved. The broad method claims do not require the precise and active steps and reagents thus, one of ordinary skill in the art would be required to determine the appropriate reagents and conditions required to achieve the claimed method. Therefore, the guidance presented is narrowly tailored to the working examples and not to the broad claims. The prior art states that only yeast cells were enabled at the time of applicants' invention. Thus, applicants' pointing to articles written well after the priority date of the instant invention drawn to non-yeast host are not persuasive.

Applicants' broadly state that each individual aspect of the claims would have been routine to one skilled in the art, however it is the examiner's position that without the exact and precise method steps and specific reagents the claimed detection and purification methods could not be achieved. Moreover, applicants' own disclosure supports that without exact and precise method steps and specific reagents the claimed detection and purification methods could not be achieved.

Moreover, the claim language drawn to heterologous nucleic acids encoding one or more subunits of a biomolecule complex embraces sequences without disclosing the actual nucleic acid sequences. Applicants urge that a skilled person could easily identify a corresponding nucleic acid. However, the claims are not enabled to embrace limitless heterologous nucleic acids. It is noted that the claims comprise one or more heterologous nucleic acids without any limit, therefore without specific information regarding the heterologous nucleic acids, one of skill in the art could not predict which heterologous nucleic acids would result in the desired encoded one or more subunits of a biomolecule complex, thereby requiring undue experimentation. Therefore, despite applicants' assertion to the contrary, one of skill in the art would be required to perform undue experimentation to use the claimed method for detecting and/or purifying biomolecules and/or protein complexes. Therefore, one skilled in the art could not make and/or use the invention without undue experimentation and the rejection is maintained. Applicants generalization that no undue experimentation is required is not found persuasive in view of the quantity of experimentation, lack of guidance and working examples and the state of the prior art. Therefore the rejection is maintained.

4. The written description rejection of claims 1-11 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained for reasons already of record. The rejection was on the grounds that the specification and claims lack sufficient written description of the generically claimed an expression

environment containing one or more heterologous nucleic acids encoding one or more subunits of a biomolecule complex.

Applicants' urge that the one of ordinary skill in the art would clearly understand how to provide an expression environment containing one or more heterologous nucleic acids encoding one or more subunits of a biomolecule complex. However, it is noted that the one or more heterologous nucleic acids are defined by their activity or function, i.e., the ability to encode one or more subunits of a biomolecule complex and does not describe the one or more heterologous nucleic acids. As previously stated, the encoding distinction is a purely functional distinction and a description of the heterologous nucleic acid by what it does, such as encoding one or more subunits of a biomolecule complex is insufficient. The written description of the one or more heterologous nucleic acids encoding one or more subunits of a biomolecule complex is insufficient when the specification fails to disclose an example of heterologous nucleic acid sequences that can be used in the claimed method.

The specification does not provide evidence that a single heterologous nucleic acid, as claimed, functions with the ability to encoded one or more subunits of a biomolecule complex. And applicants have not provided evidence to the contrary. The instant specification and claims are encompassing currently unknown sequences and claims that these nucleic acid sequences can be used to in the method of detection and purification. Therefore is evident that other heterologous nucleic acids have not yet been identified. Moreover, the instant specification fails to disclose specific heterologous nucleic acid sequences; rather the specification broadly defines the sequences to be

any and every nucleic acid sequence without any discretion. In view of the lack of evidence, it is apparent that Applicants were not in possession of all or many heterologous nucleic acid sequences that encode one or more subunits of a biomolecule complex at the time of filing the instant application. The skilled artisan cannot envision the detailed structure of a method for detecting and/or purifying biomolecule and/or protein complexes in the method comprising providing an expression environment containing one or more heterologous nucleic acids encoding one or more subunits of a biomolecules complex. Thus conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation despite applicants' assertions to the contrary.

Thus, the one or more heterologous nucleic acids described only by their ability to encode fails to meet the written description requirements. Therefore the full breadth of the claims meets the written description provision of 35 USC 112, first paragraph and the rejection is maintained.

5. The rejection of claims 1-11 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is maintained. The preamble of the claims is drawn to a method for detecting and/or purifying biomolecules and/or protein complexes, and recites purification and detection in the alternative. However the amended steps recite and require both a purification step and a detection step. Therefore, the body of the

claims recites both steps even though the preamble recites alternative language. Thus, appropriate claim language is required to make the preamble and the body of the claim commensurate in scope.

Conclusion

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ja-Na Hines
October 20, 2004

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